SEQUENCE LISTING

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<120> CONJUGATES COMPRISING HUMAN IL-18 AND SUBSTITUTION MUTANTS THEREOF

<130> PU60053

<140> 10/823,964
<141> 2004-04-14

<150> 60/462,947
<151> 2003-04-15

<160> 28

<170> FastSEQ for Windows Version 4.0

<210> 1
<211> 157
<212> PRT
<213> Homo sapiens

<400> 1

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 1               5                  10                  15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
            20                  25                  30
Met Thr Asp Ser Asp Cys Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
        35                  40                  45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
    50                  55                  60
Ser Val Lys Cys Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65                  70                  75                  80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
                85                  90                  95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
            100                 105                 110
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
        115                 120                 125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu
    130                 135                 140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
145                 150                 155
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<210> 2
<211> 157

<212> PRT
<213> Mus musculus

<400> 2
Asn Phe Gly Arg Leu His Cys Thr Thr Ala Val Ile Arg Asn Ile Asn
 1   5   10   15
Asp Gln Val Leu Phe Val Asp Lys Arg Gln Pro Val Phe Glu Asp Met
            20   25   30
Thr Asp Ile Asp Gln Ser Ala Ser Glu Pro Gln Thr Arg Leu Ile Ile
        35   40   45
Tyr Met Tyr Lys Asp Ser Glu Val Arg Gly Leu Ala Val Thr Leu Ser
    50   55   60
Val Lys Asp Ser Lys Met Ser Thr Leu Ser Cys Lys Asn Lys Ile Ile
65   70   75   80
Ser Phe Glu Glu Met Asp Pro Pro Glu Asn Ile Asp Asp Ile Gln Ser
                85   90   95
Asp Leu Ile Phe Phe Gln Lys Arg Val Pro Gly His Asn Lys Met Glu
            100   105   110
Phe Glu Ser Ser Leu Tyr Glu Gly His Phe Leu Ala Cys Gln Lys Glu
        115   120   125
Asp Asp Ala Phe Lys Leu Ile Leu Lys Lys Lys Asp Glu Asn Gly Asp
    130   135   140
Lys Ser Val Met Phe Thr Leu Thr Asn Leu His Gln Ser
145   150   155

<210> 3
<211> 203
<212> PRT
<213> Homo sapiens

<400> 3
Met His His His His His His Thr Arg Gly Met Ala Ala Glu Pro Val
 1   5   10   15
Glu Asp Asn Cys Ile Asn Phe Val Ala Met Lys Phe Ile Asp Asn Thr
            20   25   30
Leu Tyr Phe Ile Ala Glu Asp Asp Glu Asn Leu Glu Ser Asp Tyr Phe
        35   40   45
Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn Asp Gln
    50   55   60
Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp Met Thr
65   70   75   80
Asp Ser Asp Cys Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile Ile Ser
                85   90   95
Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile Ser Val
            100   105   110
Lys Cys Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile Ile Ser
        115   120   125
Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys Ser Asp
    130   135   140
Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys Met Gln
145   150   155   160
Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu Lys Glu

                165   170   175
Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu Gly Asp
            180   185   190

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Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
        195                 200


<210> 4
<211> 157
<212> PRT
<213> Homo sapiens

<220>
<223> Whereby the Cysteine at position 38 of this human IL-18
      sequence has been replaced with Serine.

<400> 4
Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
 1               5                  10                  15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
            20                  25                  30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
        35                  40                  45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
    50                  55                  60
Ser Val Lys Cys Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65                  70                  75                  80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
                85                  90                  95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
            100                 105                 110
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
        115                 120                 125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu
    130                 135                 140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
145                 150                 155


<210> 5
<211> 157
<212> PRT
<213> Homo sapiens

<220>
<223> Whereby the Cysteine at position 38 of this human IL-18
      sequence has been replaced with Serine, the Cysteine at
      position 68 has been replaced with Aspartic acid, and the
      Asparagine at position 78 has been replaced with Cysteine.

<400> 5
Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
 1               5                  10                  15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
            20                  25                  30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
        35                  40                  45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
    50                  55                  60
```

```
Ser Val Lys Asp Glu Lys Ile Ser Thr Leu Ser Cys Glu Cys Lys Ile
65                  70                  75                  80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
                85                  90                  95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
            100                 105                 110
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
        115                 120                 125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu
    130                 135                 140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
145                 150                 155
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<210> 6
<211> 157
<212> PRT
<213> Homo sapiens

<220>
<223> Whereby the Cysteine at position 38 of thi human IL-18 sequence has been replaced with Serine, the Cysteine at position 68 has been replaced with Aspartic acid, and the Glutamic acid at position 121 has been replaced with Cysteine.

<400> 6

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Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
 1                5                  10                  15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
            20                  25                  30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
        35                  40                  45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
    50                  55                  60
Ser Val Lys Asp Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65                  70                  75                  80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
                85                  90                  95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
            100                 105                 110
Met Gln Phe Glu Ser Ser Ser Tyr Cys Gly Tyr Phe Leu Ala Cys Glu
        115                 120                 125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu
    130                 135                 140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
145                 150                 155
```

<210> 7
<211> 157
<212> PRT
<213> Homo sapeins

<220>
<223> Whereby the Cysteine at position 38 of this human IL-18 sequence has been replaced with Serine, the Cysteine at position 68 has been replaced with Aspartic acid, and the Leucine at position 144

has been replaced with Cysteine.

<400> 7

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Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
 1               5                  10                  15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
            20                  25                  30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
        35                  40                  45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
    50                  55                  60
Ser Val Lys Asp Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65                  70                  75                  80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
                85                  90                  95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
            100                 105                 110
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
        115                 120                 125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Cys
    130                 135                 140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
145                 150                 155
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<210> 8
<211> 157
<212> PRT
<213> Homo sapiens

<220>
<223> Whereby the Cysteine at position 38 of the human IL-18 sequence has been replaced with Serine, the Cysteine at position 68 has been replaced with Aspartic acid, and Aspartic acid at position 157 has been replaced with Cysteine.

<400> 8

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Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
 1               5                  10                  15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
            20                  25                  30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
        35                  40                  45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
    50                  55                  60
Ser Val Lys Asp Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65                  70                  75                  80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
                85                  90                  95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
            100                 105                 110
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
        115                 120                 125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu
    130                 135                 140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Cys
145                 150                 155
```

<210> 9
<211> 157
<212> PRT
<213> Homo sapeins

<220>
<223> Whereby the Cysteine at position 38 of the human IL-18 sequence has been replaced with Serine, the Cysteine at position 68 has been replaced with Serine, and Leucine at position 144 has been replaced with Cysteine.

<400> 9
Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
1 5 10 15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
20 25 30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
35 40 45
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
50 55 60
Ser Val Lys Ser Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65 70 75 80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
85 90 95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
100 105 110
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
115 120 125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Cys
130 135 140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Asp
145 150 155

<210> 10
<211> 157
<212> PRT
<213> Homo sapiens

<220>

<223> Whereby the Cysteine at position 38 of the human IL-18 sequence has been replaced with Serine, the Cysteine at position 68 has been replaced with Serine, and Aspartic acid at position 157 has been replaced with Cysteine.

<400> 10
Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn
1 5 10 15
Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp
20 25 30
Met Thr Asp Ser Asp Ser Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile
35 40 45

```
Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile
    50                  55                  60
Ser Val Lys Ser Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile
65                  70                  75                  80
Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys
                85                  90                  95
Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys
            100                 105                 110
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
        115                 120                 125
Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu
    130                 135                 140
Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu Cys
145                 150                 155
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<210> 11
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated wild type IL-18

<400> 11
Tyr Phe Gly Lys
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<210> 12
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated wild type IL-18

<400> 12
Leu Glu Ser Lys
 1

<210> 13
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated wild type IL-18

<400> 13

Leu Ser Val Ile Arg
1 5

<210> 14
<211> 26
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 14
Asn Leu Asn Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro Leu
1 5 10 15
Phe Glu Asp Met Thr Asp Ser Asp Cys Arg
20 25

<210> 15
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 15
Asp Asn Ala Pro Arg
1 5

<210> 16
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 16
Thr Ile Phe Ile Ile Ser Met Tyr Lys
1 5

<210> 17
<211> 5
<212> PRT
<213> Artificial Sequence

<220>

<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 17
Asp Ser Gln Pro Arg
1 5

<210> 18
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 18
Gly Met Ala Val Thr Ile Ser Val Lys
1 5

<210> 19
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 19
Ile Ser Thr Leu Ser Cys Glu Asn Lys
1 5

<210> 20
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 20
Ile Ile Ser Phe Lys
1 5

<210> 21
<211> 9
<212> PRT

<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 21
Glu Met Asn Pro Pro Asp Asn Ile Lys
1 5

<210> 22
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 22
Ser Asp Ile Ile Phe Phe Gln Arg
1 5

<210> 23
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 23
Ser Val Pro Gly His Asp Asn Lys
1 5

<210> 24
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 24
Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu
1 5 10 15
Lys

<210> 25
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 25
Asp Leu Phe Lys
1

<210> 26
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 26
Leu Ile Leu Lys
1

<210> 27
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 27
Glu Asp Glu Leu Gly Asp Arg
1 5

<210> 28
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Tryptic peptides predicted for S-carboxymethylated
wild type IL-18

<400> 28
Ser Ile Met Phe Thr Val Gln Asn Glu Asp
 1   5   10